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Development of a high-performing, cost-effective and inclusive Afrocentric predictive model for stroke: a meta-analysis approach

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Abstract

Background Predicting stroke risk is critical for preventive interventions. Most validated prediction models do not include data from African populations and may not be appropriate for the region. Relying solely on statistical significance to identify predictors may compromise algorithm performance. Also, some of the existing models include expensive biomarkers that are unsuitable for resource-limited settings. This study aims to develop a cost-effective and inclusive Afrocentric predictive model for stroke (CAPMS).

Methods We conducted a meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol and searched the PubMed, Scopus, African Journal, Medline, Cochrane Library, Web of Science, and Cumulative Index for Nursing and Allied Health Literature databases. We included case–control and cohort studies reporting stroke risk factors and their estimates among African populations. Titles and abstracts were independently screened. Meta-analyses were performed using Comprehensive Meta-analysis version 3.

Results More than 50% of the eligible studies examined both ischemic and hemorrhagic stroke. More than 20 stroke risk factors were identified in Africa, with 18 eligible for meta-analysis. Homocysteine (risk weight [Rw] = 13.9, risk stability index [Ri] = 0.67), hypertension (Rw = 5.6, Ri = 0.94), and cardiac events (Rw = 3.1, Ri = 0.8) were the strongest independent predictors. Low green vegetable consumption (Rw = 2.4, Ri = 1.0), stress (Rw = 1.76, Ri = 1.0), and hypertension were the most clinically responsive risk factors. All risk factors/biomarkers except homocysteine cost between $2.8 and 12.2, indicating cost-effectiveness. A critical risk point of 12.7 was set at the 90th percentile. The cumulative Rw and costs for CAPMS 1 (20 and $1.2–4.6) and CAPMS 2 (22.4 and $6.5–17.3) indicate high performance and cost-effectiveness.

Conclusions Targeted screening via the CAPMS 1 and CAPMS 2 models offers a cost-effective solution for stroke screening in African clinics and communities. Immediate validation of the CAPMS is needed to evaluate its performance, feasibility, and acceptability in the region.

Registration The study protocol is registered with PROSPERO (ID: CRD42023430437).

Keywords Stroke, Cardiovascular disease, Prediction, Secondary prevention, Africa

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Introduction

Strokes are a major global health concern, ranking second in mortality and third in disability [1]. Annually, 15 million people worldwide suffer from stroke, resulting in 5 million deaths and disability [2]. Geographical disparities exist in age-standardized stroke incidence, mortality, prevalence, and disability-adjusted life year rates, with low- and middle-income countries (LMICs), particularly in sub-Saharan Africa, accounting for more than 80% of global stroke deaths, a burden projected to rise [3, 4]. While stroke incidence has declined by 42% in high-income countries (HICs) over four decades, it has more than doubled in LMICs [5, 6], reflecting variations in etiology, risk factors, preventive care, and funding [7]. HICs have better access to research funding, healthcare insurance, and preventive care, whereas African countries focus primarily on curative care [8]. The Eastern North Carolina study, involving 4900 community outreach risk factor screenings from 2007–2011, demonstrated a 12% higher stroke mortality rate than the rest of the state, emphasizing the importance of preventive strategies [9].

A regional shift from curative to preventive approaches is expected, aligning with Sustainable Development Goal target 3.4 [10]. Effective prevention requires adequate characterization and stratification of traditional and emerging risk factors [4, 11]. Globally, major stroke risk factors include atrial fibrillation, hypertension, dyslipidemia, and diabetes mellitus [12]. Risk assessment models, such as the Framingham risk score, have been developed to predict stroke [13], but there is only one Afrocentric model [4]. All the models have limitations, including a lack of systematic risk factor stratification, cultural insensitivity, and cost-ineffectiveness, leading to clinically inconsequential risk variables and limited external validity and accessibility [11, 14].

The existing Afrocentric model was built on Nigerian and Ghanaian data and included seven factors [4]. Despite the advances offered by Akpa and colleagues [4] for effective clinical prediction of stroke in the African context, the reliability of the Afrocentric model is questionable. The African race is the world's largest population of black people and is heterogeneous [15]. In 2009, a genetic clustering study that genotyped 1327 polymorphism markers in different African populations reported fourteen ancestral groups that share cultural or linguistic orientations and correlate with self-described ethnicity [16]. In the 2018 global whole-genome sequencing study, similar groups were reported across different African populations [16]. In both genetic studies, the ancestral clusters were well represented in at least one or more regions of North Africa, Eastern Africa, and West and Southern Africa [17], Fig. 1. Thus, an Afrocentric stroke model should represent all African regions that are home to various ancestral groups. Such models should include factors that represent risk factors for stroke in at least three traditional African regions. Consequently, we aimed to develop an Afrocentric predictive model for stroke using a novel evidence synthesis approach to ensure inclusiveness and cost-effectiveness.

Population, exposure, comparison, outcome, and timeframe (PECOT) criteria.

The review included individuals without stroke but with known exposure status, followed prospectively until stroke occurrence; individuals without stroke but with known exposure status at initial care, followed retrospectively for stroke cases; or individuals with or without stroke assessed for exposures, as in a case–control study [19]. The primary outcomes were stroke risk factors such as hypertension, obesity, diabetes, age, and smoking, along with risk estimations and a bias risk score. Additional outcomes included derived risk estimates, such as the risk stability index (Ri) and risk weight (Rw) [11]. The review covered the period from the inception of the oldest database (1961) to May 10, 2023.

Aim

To develop an Afrocentric predictive model for stroke using a novel evidence synthesis approach to ensure inclusiveness and cost-effectiveness.

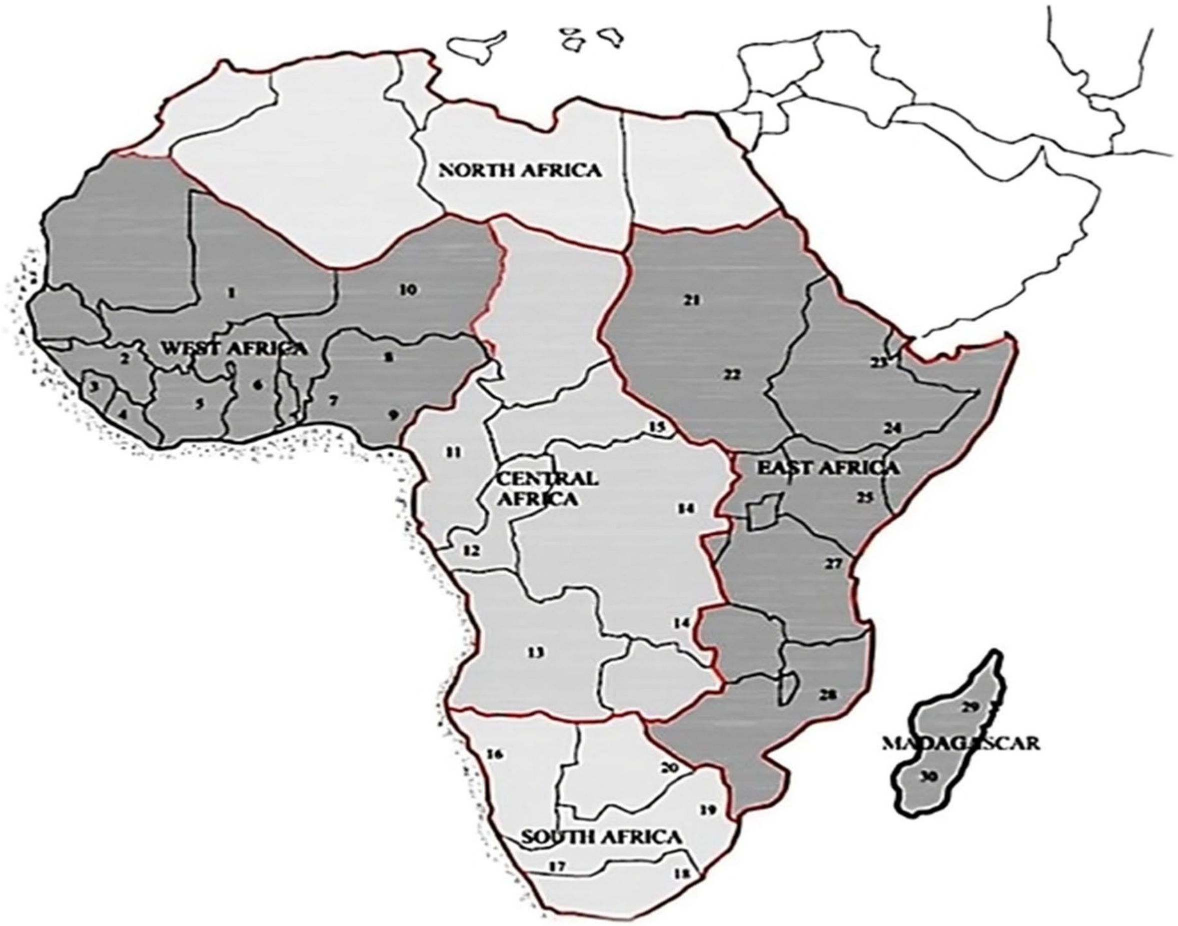
Objectives:

1. Identify the traditional and emerging risk factors for stroke in Africa
2. Determine the aggregate risk estimate for each of the identified stroke risk factors
3. Determine the relative risk weight for each of the identified risk factors
4. Determine the spatial distribution of the identified stroke risk factors in Africa
5. Determine the cost of assessing each of the identified stroke risk factors in Africa
6. Determine the critical risk threshold for the detection of stroke in Africa
7. Assemble a cost-effective Afrocentric predictive model for stroke based on the critical risk threshold

Methods

Design

This systematic review with meta-analysis is registered with the International Prospective Register of Systematic Reviews (PROSPERO; ID: CRD42023430437). This review employed meta-analysis to develop an Afrocentric clinical predictive model for stroke. The protocol followed the PRISMA checklist [20] and adhered to MOOSE recommendations [21].



S/N	WEST AFRICA	S/N	CENTRAL AFRICA	S/N	SOUTH AFRICA	S/N	EAST AFRICA/ MADAGASCAR
1	Dogon	11	Fang & Kuba	16	San & others	21	Dikur & Nuer
2	Baga	12	Kongo	17	Tsotho	22	Bongo
3	Mende	13	Chokwe	18	Zulu	23	Konso
4	Baude & Senfo	14	Luba	19	Tonga	24	Masai
5	Fante	15	Lega	20	Shona	25	Swahili
6	Fon					26	Turkana & Iraqw
7	Yoruba					27	Samburu & Pokot
8	Hausa					28	Zaramo
9	Igbo					29	Chewa
10	Bamana					30	Sakalava

Fig. 1 Africa showing major ethnic clusters and regions. Source. Adapted from Saylor [18]

Eligibility criteria

Inclusion criteria

Studies were included if they (1) were peer-reviewed African studies; (2) examined stroke patient risk factors; (3) employed case–control, cohort design, or systematic review of these designs; (4) had a low or moderate risk of bias; (5) reported risk factors and corresponding risk estimates (odds ratios [ORs]) or provided sufficient data to calculate these risk factors; (6) were published in English or French; and (7) reported the risk factors in at least three studies for meta-analysis inclusion. There were no restrictions on publication country, race, or sex.

Exclusion criteria

Studies were excluded if they were (1) cross-sectional, (2) presented a high risk of bias, (3) were published in languages other than English and French, or (4) lacked a risk estimate (e.g., ORs) despite reporting the prevalence of stroke risk factors.

Exposure and outcome measures

The outcome measures included laboratory and nonlaboratory-based measures. The exposures were stroke risk factors and corresponding risk estimates. Stroke risk factors may include hypertension, obesity, atrial fibrillation, and inadequate physical activity, among others.

Sources of information

Medline**,** PubMed, the Cochrane Library, the Cumulative Index for Nursing and Allied Health Literature (CINAHL), Web of Science, Scopus and the African Journal (SABINET) were searched from 1966 to May 10, 2023. A draft MEDLINE search strategy developed by the subject librarian (SNM) and the primary investigator (MN) is provided in Appendix 1.

Search strategy development

The subject librarian (SNM) and the primary investigator (MN) created and optimized a search strategy on the basis of key concepts and medical subject categories. A PubMed pilot search was used to assess the appropriateness of the search strings (Appendix 1). The terms were modified for database-specific syntax and subject headings across multiple databases. MeSH terms, keywords, wildcards, truncation, and Boolean operators were employed to search title, abstract, and keyword fields, ensuring thorough results.

Data management

The results retrieved for the literature search were exported to EndNote 20, and duplicates were eliminated. After removing duplicates, titles and abstracts were screened.

Study selection and data extraction

The principal investigator (MN) and coauthor (PO) conducted the initial title and abstract screening. Discrepancies between MN and PO were resolved through discussions. PO extracted data, which MN subsequently verified. No corresponding authors of the full-text articles were contacted since the necessary information was available in the texts. The PRISMA diagram outlines the study selection process and reasons for exclusion (Fig. 2).

Data items

The primary data included risk factors and their corresponding estimates (ORs) as well as risk of bias scores and subsequently included Ri, Rw, and critical risk point (CRP). The secondary data included study characteristics such as type of stroke, setting, study design, and sample size.

Risk of bias assessment

We evaluated the risk of bias in case–control and cohort studies using the Joanna Briggs Institute tools [22]. MN and PO independently rated 20% of the studies, achieving high interrater agreement. Interrater agreement was calculated by the ratio of mutually accurately rated articles to the total number of articles examined. PO reviewed the remaining 80% of the studies.

Effect measures

The means and standard deviations were used to describe the quantitative characteristics of the participants in the included studies. The participants'educational achievements and sex are summarized as percentages. The CRP was calculated in line with the methods of Nweke et al. [11] and Nwagha & Nweke [23].

Data synthesis and analysis

Risk estimates were standardized to ORs for comparison [24, 25], using 1/OR for OR < 1 to standardize the effect direction [26] and adjusting the confidence interval using [$1/OR^2$]. Aggregated ORs, heterogeneity (I^2), and publication bias for each risk factor were estimated via a random-effects meta-analysis model. The inverse variance method in Comprehensive Meta-Analysis (CMA) software identified CRPs in the fourth quartile. Meta-analyses were conducted using CMA (version 4) and SPSS, with $\alpha = 0.05$ as the significance level.

Determining the risk responsiveness and risk weight of the identified risk factors

Risk responsiveness (Ri) denotes the proportion of studies reporting a specific risk factor as significant, expressed as $f_s/\sum f$. It measures the consistency of a factor being reported as a risk factor, assuming no publication bias or selective reporting. Rw is a product of the risk estimate (ORs) and Ri, which was calculated as $Rw = OR \times Ri$.

Examining the spatial distribution of stroke risk factors in Africa

A risk factor was considered Afrocentric if the supporting data came from at least three countries from three of the four African regions. Exceptions were made for emerging stroke risk factors and those requiring high investigation costs. We ensured that 75% of the risk factors in each model met these three-out-of-four criteria.

Determining the critical risk point

The CRP on a risk curve indicates when a disease or outcome is imminent, thus necessitating preemptive

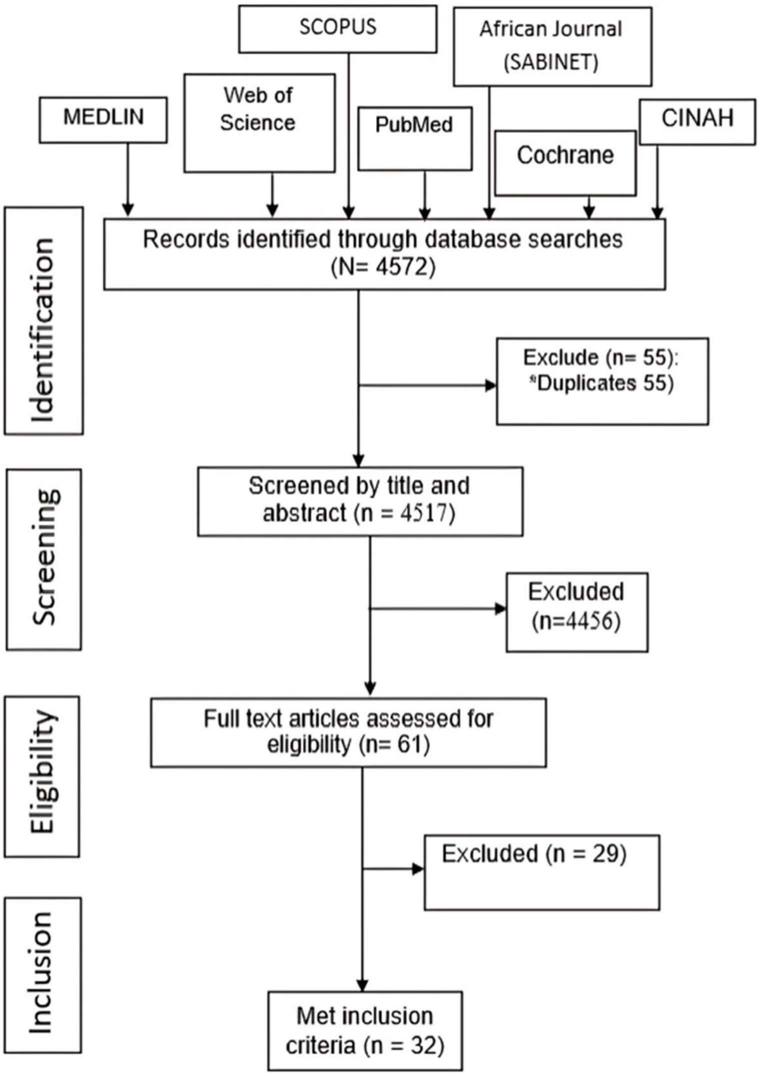


Fig. 2 PRISMA flow diagram of the meta-analysis of the risk factors for stroke in Africa (1996–2022)

interventions, such as a high-risk preventive strategy. In such strategies or targeted screening, the CRP lies in the upper-risk quartile (76 th to 100 th percentile) of the Rw distribution and captures the most clinically relevant markers. The risk points were divided into four quartiles: first (0–25%), second (26–50%), third (51–75%), and fourth (76–100%), corresponding to the lowest, lower, middle, and upper-risk factor classes, respectively.

Determining cost-effectiveness

Determining the CRP enables the development of a cost-effective model using a prudent combination of clinically relevant and responsive risk factors/biomarkers [23, 27]. Prudence was defined in terms of cost-effectiveness and the critical risk threshold. Cost-effectiveness was estimated on the basis of the average investigative cost of putative model factors or biomarkers in representative African regions. Data on the costs of investigating risk factors were collected from laboratories in Nigeria, South Africa, Tunisia, and Tanzania, with prices adjusted for inflation using dollar-to-currency mid-rate histories [28]. A risk factor or model was considered cost-effective if the investigative cost was within 175% of the average price.

Results

Study selection and characteristics

After 4517 records were identified and screened, 32 articles (27 case–control, 5 cohort, and one systematic review) involving 38,544 African participants were included (Fig. 2). Studies were conducted in West Africa

(39.4%), North Africa (36.4%), East Africa (9%), and sub-Saharan Africa [29], across all African regions [30, 31], and East and Southern Africa [32, 33]. Studies examined ischemic and hemorrhagic stroke (51.5%), ischemic stroke only (42.4%), or hemorrhagic stroke only (6%) (Table 1). The meta-analysis included 26 articles on 18 risk factors (Fig. 2), excluding factors reported once or twice, such as regular sugar consumption, history of stroke, unemployment, specific alleles, and depression (Appendix 2).

Risk factors and categories of stroke

Eighteen studies investigated hypertension as a risk factor, with 12 focusing on both ischemic and hemorrhagic stroke, five on ischemic stroke, and one on hemorrhagic stroke. Seventeen studies analyzed diabetes, 10 considered both stroke types, six analyzed ischemic stroke, and one analyzed hemorrhagic stroke. Twelve studies on dyslipidemia included nine on both stroke types, seven on ischemic stroke, and one on hemorrhagic stroke. Fourteen studies investigated smoking, 11 included both stroke types, two included ischemic stroke, and one included hemorrhagic stroke. Ten studies reported cardiac causes, eight on both stroke types and two on ischemic stroke. Seven studies examined alcohol consumption, six on both stroke types and one on ischemic stroke. Six studies identified physical activity as a risk factor for both stroke types. Ten studies examined obesity, eight examined both stroke types, and two examined ischemic stroke. Six studies reported stress, four on both stroke types, one on ischemic stroke, and one on hemorrhagic stroke. Eight studies noted age, with six on both stroke types and two on ischemic stroke. Appendices 2 and 3 provide detailed distributions of stroke categories for these risk factors.

Risk stratification and the critical risk point

Age, sex, and education were nonresponsive (Ri <0.5), whereas hyperhomocysteinemia (Rw =13.9, Ri =0.67) and hypertension (Rw =5.6, Ri =0.94) were significant risk factors for stroke. Low green vegetable consumption and hypertension had the greatest effects (Ri =1.0 and 0.94, respectively). Other risk factors included cardiac disease (Rw =3.1, Ri =0.8), diabetes (Rw =2.5, Ri =0.76), low green vegetable consumption (Rw =2.4, Ri =1.0), dyslipidemia (Rw =2.4, Ri =0.83), high stress (Rw =1.76, Ri =1.0), and HIV (Rw =1.70, Ri =0.67). Low high-density lipoprotein (HDL) (Rw =3.3) and high total cholesterol (1.70) are key indicators of dyslipidemia. Assuming that the CRP lies in the upper quartile distribution of the risk weights, the 76 th percentile (12.7) was sufficient to accommodate as many risk factors as possible (Table 2).

Spatial distribution of risk factors for stroke in Africa

The meta-analysis identified 18 risk factors, 15 of which were clinically relevant. Hypertension, diabetes, cardiac causes, smoking, alcohol consumption, physical inactivity, obesity, stress, and dyslipidemia were common across all regions, whereas HIV was a risk factor in all three regions. Family history of cardiovascular disease, added table salt, and low green vegetable consumption as risk factors for stroke were investigated in West Africa only. Hyperhomocysteinemia is a risk factor in West and North Africa. Data on sub-African ethnicities were scarce (Appendix 3).

Cost of investigating relevant risk factors in USD

To determine cost-effectiveness, we estimated the costs of investigating selected biomarkers from Nigeria, South Africa, Tunisia, and Tanzania and calculated the average price. A biomarker was deemed cost-effective if the cost was within the average of $7.5. Conversely, a biomarker or model was considered not cost-effective if the investigation cost exceeded the average price by 75% ($7.5). All biomarkers except homocysteine were identified as cost-effective, with prices ≤$12.6 (Table 3).

Assembling the models and model components

Table 4 lists the emerging models, all of which meet the CRP. However, only two models, CAPMS 1 and CAPMS 2, were deemed cost-effective, with associated investigation costs of $1.2–4.6 and $7.7–21.9, respectively (Appendices 4 and 5). Hyperhomocysteinemia was the only univariate model (Table 4). CAPMS 1 includes hypertension, high stress levels, diabetes, smoking, and low consumption of leafy vegetables (Appendix 4). The scoring details are presented in Appendix 4. CAPMS 2 encompasses dyslipidemia, hypertension, high stress levels, smoking, diabetes, low consumption of leafy vegetables, HIV status, and a family history of cerebrovascular disease (Appendix 5). The scoring details are presented in Appendix 5. Unlike existing stroke risk assessment tools from case−control or cohort studies, the CAPMS model components are derived from meta-analyses of 18 risk factors involving over 33,000 Africans. Risk factor selection was rigorous and was based on the clinical relevance measured by the critical Rw and the clinical minimum important change.

Examining preexisting models versus our study findings

There are three main issues with the current risk assessment tools: lack of data from Africa, poor suboptimal predictive potential (CRP <12.7), or high costs. The CUORE, SCORE, nonlaboratory NHANES, and MUCA models have insufficient predictive power. The

Table 1 Characteristics of the studies included in the review

Authors	Study Design	Method of data collection	Stroke type	Sample size	Country	Region
Akpalu et al. [34]	Case–control	Retrospective	Ischemic and intracerebral hemorrhage	3553	Nigeria and Ghana	West Africa
Elagib et al. [35]	Case–control	Retrospective	Thrombotic CVA	400	Sudan	North Africa
O'Donnell et al. [30]	Case–control	Prospective	Ischemic and intracerebral hemorrhage	1949	Africa (Mozambique, Nigeria, South Africa, Sudan, and Uganda)	All regions
Owolabi [36]	Case–control	Retrospective	Ischemic and hemorrhagic	252	Nigeria	West Africa
Owolabi [37]	Cohort	Retrospective	Ischemic	702	Nigeria	West Africa
Chehaibi et al. [38]	Case–control	Retrospective	Ischemic	388	Tunisia	North Africa
de Mast et al. [39]	Case–control	Retrospective	Ischemic	527	Tanzania	East Africa
Fekih-Mrissa et al. [40]	Case–control	Retrospective	Ischemic	184	Tunisia	North Africa
Saidi et al. [41]	Case–control	Retrospective	Ischemic and hemorrhagic	773	Tunisia	North Africa
Saidi et al. [42]	Case–control	Retrospective	Ischemic	498	Tunisia	North Africa
Saidi et al. [43]	Case–control	Retrospective	Ischemic and hemorrhagic	253	Tunisia	North Africa
Akpa et al. [4]	Case–control	Retrospective	Ischemic and hemorrhagic	7066	Ghana and Nigeria	West Africa
Akpalu et al. [44]	Case–control	Retrospective	Ischemic and hemorrhagic	1998	Ghana	West Africa
Amu et al. [45]	Case–control	Prospective	Ischemic, intracerebral and subarachnoid hemorrhage	160	Nigeria	West Africa
Diakite et al. [46]	Case–control	Retrospective	Ischemic	381	Morocco	North Africa
Diakite et al. [47]	Case–control	Retrospective	Ischemic	376	Morocco	North Africa
Fekadu et al. [48]	Cohort		Ischemic and hemorrhagic	116	Ethiopia	East Africa
O'Donnell et al. [31]	Case–control	Prospective	Ischemic and hemorrhagic	646	Africa (Mozambique, Nigeria, South Africa, Sudan, and Uganda)	All regions
Saidi et al. [49]	Case–control	Retrospective	Ischemic stroke	551	Tunisia	North Africa
Okubadejo et al. [50]	Case–control	Prospective	Ischemic stroke	115	Nigeria	West Africa
Chang et al. [33]	Case–control	Prospective	Ischemic and hemorrhagic	772	Africa (Kenya, Zambia, Zimbabwe)	Southern Africa
Poulter et al. [32]	Case–control	Prospective	Ischemic	56	Africa (Kenya, Zambia, Zimbabwe)	Southern Africa
Mbonde et al. [51]	Cohort	Prospective	Intracerebral hemorrhage	73	Uganda	East Africa
Namale et al. [28]	Systematic review	Systematic review	Ischemic and hemorrhagic	2003	Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cape Verde, Central Africa, Republic, Chad etc	Sub-Saharan Africa
Saidi et al. [52]	Case–control	Retrospective	Ischemic stroke	773	Tunisia	North Africa
Salem-Berrabah et al. [53]	Case–control	Retrospective	Ischemic stroke	147	Tunisia	North Africa
Sarfo et al. [54]	Cohort	Prospective	Ischemic and hemorrhagic	3296	Ghana	West Africa
Sarfo et al. [55]	Case–control	Retrospective	Hemorrhagic and ischemic stroke	2118	Nigeria and Ghana	West Africa
Sarfo et al. [56]	Case–control	Prospective	Hemorrhagic and ischemic stroke	1080	Nigeria and Ghana	West Africa

Table 1 (continued)

Authors	Study Design	Method of data collection	Stroke type	Sample size	Country	Region
Sarfo et al. [57]	Cohort	Prospective	Ischemic and hemorrhagic stroke	1365	Ghana	West Africa
Sarfo et al. [58]	Case–control	Retrospective	Intra cerebral hemorrhage	2944	Ghana and Nigeria	West Africa
Sarfo et al. [59]	Case–control	Retrospective	Ischemic stroke	2431	Ghana and Nigeria	West Africa
Walker et al. [60]	Case–control	Prospective	Ischemic and hemorrhagic	598	Tanzania	North Africa

Framingham, PROCAM, Reynolds risk score, QRISK, CHSCO, ARIC, and SMART-REACH models are predictive but expensive for LMICs. The Self-Reported Stroke Risk Stratification Scale (ASSIGN), Zhao's Risk Stratification Tool for Ischemic Stroke, and NHANES laboratory models are predictive and cost-effective but do not represent African populations. Akpa's Afrocentric approach, originating from West Africa, is predictive and affordable but time-consuming (Table 5).

Discussion

Stroke risk assessment tools face challenges such as limited African data, a lack of responsiveness stratification, and cost-ineffectiveness. This study develops cost-effective Afrocentric models, CAPMS 1 and CAPMS 2, which are expected to reduce false negative and positive rates compared with existing models. Identifying multiple biomarker combinations that meet the threshold improves individuality and cost-effectiveness, particularly in Africa, where high costs can limit access to biomarker investigations. Further research is needed to confirm these findings, and existing models may need to be recalibrated. Accurately predicting stroke would enhance preventative measures and patient selection for randomized trials [80, 81]. This work proposed two alternative models for use in Africa, with the justification for the inclusion of the identified risk factors as follows:

Elevated homocysteine (tHcy > 15 µmol/L) was a significant risk factor for stroke risk in Africa, with individuals 21 times more likely to suffer a stroke than those with normal levels, which is consistent with the findings of non-African studies [82, 83]. A meta-analysis confirmed hyperhomocysteinemia as a risk factor for initial stroke and coronary heart disease events [83]. Homocysteine, a toxic sulfur-containing intermediary in methionine metabolism [84], becomes problematic when its metabolism is impaired or when cofactors for recycling are lacking, establishing it as an independent risk factor for stroke [84–86]. Neural cells are particularly vulnerable to prolonged hyperhomocysteinemia [84]. Despite its predictive potential, the high cost of investigating hyperhomocysteinemia may limit its use in stroke screening models, and its imperfect risk responsiveness suggests that some stroke occurrences in Africa may not be related to hyperhomocysteinemia [40, 44, 50]. Understanding the clinical and economic significance of hyperhomocysteinemia could help develop a device-based screening tool for predicting stroke onset in Africa.

Hypertension, an important risk factor for stroke, is associated with high risk responsiveness and weight, reported in 94% of the articles [31, 87]. Despite its cost-effectiveness and presence in most stroke models, hypertension alone may not consistently predict ischemic stroke in Africa, where its impact could be amplified by factors such as elevated homocysteinemia, poor folate intake, dietary issues, and high sodium consumption [4, 88, 89]. The DASH diet, which emphasizes vegetables, whole grains, fruits, low-fat dairy, poultry, fish, and nuts while limiting red meat, sweets, and sugar, can effectively reduce blood pressure [90]. Therefore, stroke risk mitigation strategies for hypertensive patients should prioritize blood pressure control, nutrition, and lifestyle modifications.

Cardiac causes, such as atrial fibrillation, myocardial infarction, prosthetic heart valve, rheumatic valvular heart disease, and left ventricular failure, are independent predictors of stroke, especially ischemic stroke. This finding aligns with global data indicating that cardiac conditions, notably heart failure and atrial fibrillation, increase stroke risk by 2–5 times [91–95]. In high-income countries, investigating cardiac causes is cost-effective justifying its inclusion in most stroke predictive models. In Africa, the investigation cost is affordable only if it is the only laboratory factor in the model. Nonetheless, the strong association of cardiac causes with ischemic stroke [96] may balance the greater incidence of hypertension-linked hemorrhagic stroke [97], particularly in the development of a generic stroke model. Interestingly, nutritional and dietary factors in Africa may increase the relevance of cardiac causes in stroke pathogenesis

Table 2 Risk factors or biomarkers of stroke

Factors	Reference category	Ri	OR	95% CI	*p* value	I^2	Egger's test t value *p*		Rw (N-factor)	Rank/class
Hyperhomocysteinemia	**Abnormally elevated Hcy (Hcy > 15 micromol/L)**	**0.67**	**20.80**	**1.05–41**	**0.047**	**95.05**	**0.056**	**0.964**	**13.94**	**Upper class**
Hypertension	History of hypertension or sustained BP ≥ 140/90 mmHg for 72 h	0.94	5.94	3.93–8.98	< 0.001	95.59	2.167	0.046	5.58	Upper class
Cardiac causes (Atrial fibrillation, myocardial infarction, prosthetic heart valve, rheumatic valvular heart disease)	Previous history, review of baseline electrocardiograph results showing any heart issue	0.8	3.91	2.51–6.08	< 0.001	76.75	1.022	0.336	3.13	Upper class
Diabetes	History of diabetes or HbA1 C ≥ 6.5%	0.76	3.23	2.63–3.97	< 0.001	73.55	0.713	0.487	2.45	Upper class
Dyslipidemia	TC ≥ 5.2 mmol/L, HDL ≥ 1.03 mmol/L, LDL ≥ 3.4 mmol/L or TAG ≥.7 mmol/L	0.83	2.84	1.84–4.38	< 0.001	85.24	0.503	0.642	2.36	Upper class
HDL	HDL ≥ 1.03 mmol/L	1	2.48	0.72–8.55	< 0.001	84.11	0.381	0.768	3.3	Upper class
Total cholesterol	≥ 5.2 mmol/L	0.57	2.98	1.33–6.69	0.008	95.485	1.512	0.191	1.71	Lower middle
Triglyceride	TAG ≥ 1.7 mmol/L	0.33	1.56	1.16–2.08	0.003	< 0.001	0.029	0.982	0.51	Lower class
Low consumption of consumption of green veg	Low consumption of green leafy vegetable	1	2.44	1.87–3.19	< 0.001	49.280	0.450	0.697	2.44	Upper middle
Stress	High level of stress (combined measures of stress at home/work (e.g. irritability, anxiety or sleeping difficulties) and life events experienced in the 2 weeks preceding	1	1.76	1.48–2.08	< 0.001	31.121	0.272	0.799	1.76	Upper middle
HIV	HIV^+	0.67	2.53	1.25–5.13	0.010	69.727	0.132	0.916	1.70	Lower middle
Family history of cerebrovascular disease	YES	0.8	1.88	1.41–2.51	< 0.001	44.559	1.210	0.313	1.50	Lower middle
Smoking	Previous/current smoker	0.64	2.22	1.69–2.92	< 0.001	54.196	2.323	0.039	1.42	Lower middle
Meat consumption	Regular meat consumption	0.75	1.78	1.51–2.10	0.874	< 0.001	1.400	0.296	1.34	Lower middle
Physical inactivity	Physical inactivity (Less than 4 h moderate intensity/strenuous leisure activity per week)	0.67	1.78	1.60–1.99	< 0.001	1.975	1.493	0.210	1.19	Lower middle
Income	Monthly income < 100 USD	0.6	1.60	1.38–1.85	< 0.001	< 0.001	0.598	0.592	0.96	Lower middle
Alcohol consumption	Current alcohol consumption, especially high/heavy episodic intake (seven or more drinks per week	0.57	1.76	1.39–2.24	< 0.001	47.71	0.150	0.887	1.00	Lower middle
Obesity	BMI ≥ 30 kg/m^2	0.38	1.65	1.13–2.39	88.931	0.009	0.746	0.484	0.63	Lower class
Added table salt	Regular use of table salt	0.33	1.62	1.13–2.31	0.009	< 0.001	SE = 0	≥ 1.00	0.53	Lower class
Education	No formal education	0.25	1.32	1.01–1.62	0.009	< 0.001	1.148	0.370	0.33	Lower class
Age	NSF	0.25	1.08	0.98–1.18	0.132	70.741	2.648	0.038	0.27	Lower class
Sex	Male	0.12	1.25	1.05–1.49	0.011	< 0.001	1.449	0.221	0.15	Lower class

TAG triglycerides, *TC* total cholesterol, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *BMI* body mass index, critical risk point (95 th percentile): 12.7; first quartile: ≤ 0.61; second quartile: 0.62–1.46; third quartile: 1.47–2.44; fourth quartile: ≥ 2.5; ^{T}: met the clinical minimum important diffrerence (CMID) defined as a change in the odds ratio (OR) ≥ 0.6

Table 3 Cost of investigating relevant risk factors (putative model components) in USD

Biomarker (test)	Nigeria([1] 1$ = 770 as at 05/07/2023	South Africa (R) Rate: 1$ = R17.87 as at 22/07/2023	Tunisia (TND) Rate: 1$ = 3.09 TND as at 05/07/2023	Tanzania Rate: 1$ = 2422.7 TSHS as at 2024	The overall average median cost less homocysteine cost ($)
Blood glucose	1400 (1.8)	R82 (4.6)[b]	TND 8.6 (2.8)[c]	2812 (1.2)	$2.6
HIV	1000 (1.3)	R149 (8.3)[b]	TND 21.9 (7.1)[c]	0.00 (0.00)	$4.2
Lipid profile	5000 (6.5)	R310 (17.3)[b]	TND 32.2 (10.4)[c]	40,000 (15.5)	$12.4
ECG	3000 (3.9)	R246 (13.8)	TND 38.7 (12.5)[c]	30,000 (11.6)	$10.5
Homocysteine	37,800 (48.8)[a]	R185 (10.4)[b]	-	50,000 (19.3)	-
Mean less homocysteine	2600 (3.4)	R196.8 (9.2)	TND 25.4 (8.2)[c]	17,104 (7.1)	$7.5 ±4.7 ($2.8–12.2)

[1] USD = R17.87 as at 22/07/2023; 1 USD = 770 as at 05/07/2023; *ECG* electrocardiogram

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[a] https://healthtracka.com/panels/homocysteine-133/

[b] National Health Laboratory Service, 2018; [c]:Institut Pasteur Tunis

Table 4 Assembly of models and model components

Potential models	Components	Rw vis-à-vis CRP = 12.7	Remarks
Standalone hyperhomocysteinemia model	Hyperhomocysteinemia	13.9	Univariate & not cost-effective
CHH model	Cardiac causes, hypertension & hyperhomocysteinemia	22.8	Multivariable & not cost-effective
CaLHVeF model	Cardiac causes, dyslipidemia, high levels of stress, low consumption of leafy vegetables, hypertension	14.8	Multivariable & cost-effective
CAPMS 1	Hypertension, high stress levels, diabetes, smoking, and low consumption of leafy vegetables (Appendix 4)	20	Multivariable & cost-effective
CAPMS 2	Dyslipidemia, hypertension, high stress levels, smoking, diabetes, low consumption of leafy vegetables, family history of cerebrovascular disease and HIV (Appendix 4)	22.4	Multivariate & cost-effective

[98–100]. The high cost and inefficiency of cardiac testing may hinder its inclusion in stroke screening models, especially for those without known cardiac histories and in areas where cardiac causes are not major public health concerns. However, in African regions with high CVD prevalence [101], cardiac causes should be considered in stroke screening models. Given testing challenges, a CVD history with a risk stability index of 0.8 and an OR of 1.88 could replace field testing for cardiac causes, eliminating investigative costs. However, this approach is more suitable in communities with routine health checks, unlike many African settings where patients seek care at advanced disease stages.

Dyslipidemia, defined by specific cholesterol, HDL, low-density lipoprotein (LDL), or triglyceride levels [4], is a significant risk factor for stroke in Africa, with a Ri of 0.83, reported as significant in 83% of articles, particularly for ischemic stroke. Despite its potential utility in stroke predictive models, dyslipidemia cannot serve as a standalone predictor or biomarker owing to its high costs. Its interaction with hyperhomocysteinemia [86], hypertension [102], and heart diseases [103] supports its efficacy as a biomarker for low-risk groups. HDL is the most critical dyslipidemia cause with perfect risk responsiveness and a risk weight of 3.3, informing its inclusion in the PROCAM and ASSIGN models. Nutritional and dietary factors such as poor folate intake [98], regular meat consumption [99], alcohol consumption [100], low green vegetable intake, and high salt intake [98] may exacerbate the role of dyslipidemia in stroke pathogenesis in Africa, highlighting key targets for primary stroke prevention. Thus, coupled with its relatively low investigative cost, it is an important risk factor for predicting stroke in Africa.

Individuals with a history of diabetes or an HbA1c ≥ 6.5% are approximately three times more likely to experience a stroke since diabetes damages cerebral blood vessels through pathological changes [104]. Diabetes-induced atherosclerosis resulting from prolonged high blood sugar levels is a significant risk

Table 5 Existing stroke risk assessment models/tools

Risk assessment tool	Component factors	Criticism	The implication of the criticism versus our findings
Framingham model [61]	Age, systolic BP, hypertensive therapy, diabetes mellitus, cigarette smoking, history of coronary heart disease, presence of atrial fibrillation & left ventricular hypertrophy	Based on a small US, largely white middle-income sample [62] Only predicts future coronary heart diseases and does not predict future total cardiovascular events [62] The Framingham risk score could overestimate or underestimate risk in populations [63]	Met the CRP but not cost-effective as ECG test alone is not sufficient to suggest left ventricular hypertrophy; it will require further tests African data is not involved; hence, it may not be appropriate for the region
PROCAM model [64]	LDL cholesterol, smoking, HDL cholesterol, systolic blood pressure, family history of premature myocardial infarction, diabetes mellitus & triglycerides	Based on a sample of industrial German employees [65]. Only estimates the risk for fatal or nonfatal myocardial infarction [65]. It may be considered somewhat underpowered for risk estimation for women [65]	Met the CRP but not cost-effective Application to African populations is limited
Reynolds Risk Score [66]	Systolic BP, hypertensive therapy, diabetes mellitus, cigarette smoking, history of coronary heart disease, presence of atrial fibrillation & left ventricular hypertrophy, parental history of premature coronary heart disease & high sensitivity C- reactive protein	Derived from only two cohort studies hence its external validity is questionable [66]. Unclear whether high sensitivity c-reactive protein is a risk factor for cardiovascaulr disease (CVD), i.e., lack of stratification of risk factors [66]	Met the CRP but not cost-effective Application to the African population is limited
MUCA model [67]	Weight, height, three consecutive blood pressure readings, 12-h fasting blood sample, and blood lipids to measure total cholesterol	Model based on Chinese individuals living in China [68]	Cumulative Rw is less than the CRP (suboptimal predictive potential) Application to the African population is limited
ASSIGN [69]	Sex, age, total cholesterol, HDL cholesterol, systolic blood pressure, cigarette smoking status and deprivation, diabetes, family history of coronary heart disease	Random samples from the general population in Scotland only; hence, the external validity is questionable [69] The basis for excluding obesity or BMI is not understood, i.e., lack of stratification of risk factors Woodward et al. [69]	Met the CRP but we consider age and sex clinically insignificant factors in Africa. Application to the African population is limited
CUORE [70]	Age, systolic blood pressure, total cholesterol, smoking habit, diabetes, & hypertension therapy	Not applicable outside Italy and hence lacks external validation for global application [70]	Cumulative risk point less than CRP; hence, it may perform suboptimally in Africa. Application to the African population is limited
SCORE [71]	Patients with established disease, asymptomatic individuals at high risk of CVD mortality, first-degree relatives of patients with premature CVD & other individuals encountered during clinical practice	The scoring system only predicts the risk of CV death and does not consider nonfatal CVD events [72] The score function is only recommended for use in the 40 to 65-year age range [71] May overestimate risk in countries with decreasing CVD mortality and underestimate risk in countries with increasing CVD mortality [73]	Cumulative risk point less than CRP hence may perform suboptimally in Africa. Application to the African population is limited

Table 5 (continued)

Risk assessment tool	Component factors	Criticism	The implication of the criticism versus our findings
QRISK [65]	Age, sex, smoking, systolic blood pressure, the ratio of total serum cholesterol to HDL, BMI, family history of coronary heart disease aged less than 60 years are a measure of deprivation & existing treatment with the antihypertensive agent, ethnic origin, type 2 diabetes, rheumatoid arthritis, atrial fibrillation and chronic renal disease	The data is only from England and Wales [65] The dataset is incomplete for some risk factors; therefore, imputation and statistical modeling are needed to reduce biased estimates [65]	Met the CRP but not cost-effective Application to the African population is limited
Self-Reported Stroke Risk Stratification (SRSRSF): The Regards Study [74]	Age, race, sex, self-report of a physician diagnosis of hypertension, diabetes mellitus, atrial fibrillation, & heart disease status, current cigarette smoking, education, general self-reported health, any history of stroke symptoms as assessed by questionnaire	The major limitation is that REGARDS included only black and white participants, so it is unclear whether these findings can be generalized to other race-ethnic groups [74]	Met the CRP and cost-effective Application to the African population is limited
Risk Stratification Tool for Ischemic Stroke: A Risk Assessment Model Based on Traditional Risk Factors Combined With White Matter Lesions and Retinal Vascular Caliber [75]	Number of eyes, age, BMI, sex, height, weight, history of hypertension, hyperlipidemia, diabetes, coronary heart disease, cigarette smoking habits and consumption levels of alcohol	The included cases were collected from a single center, and the small sample limits the ability to predict stroke [75] The stroke group was derived from hospitalized patients and two subtypes of ischemic stroke; other stroke types were not included [75]	Met the CRP & cost-effective Application to the African population is limited
The Cardiovascular Health Study (CHS) Cohort [76]	Age, aspirin usage, diabetes, impaired glucose tolerance, higher systolic blood pressure, increased time needed to walk 15 ft, frequent falls, elevated creatinine levels, abnormal left ventricular wall motion and increased left ventricular mass on echocardiography, ultrasound-defined carotid stenosis, and atrial fibrillation	The CHS contains more men and African American participants [76] The external validity is not fully assessed [76]	Met the CRP but not cost-effective Application to the African population is limited
Prediction of Ischemic Stroke Risk in the Atherosclerosis Risk in Communities Study (ARIC Study) [77]	Age, race, smoking status, diabetes mellitus, left ventricular hypertrophy, previous coronary heart disease, use of antihypertensive medication, systolic blood pressure	This study included an African-American cohort from just one city [74] Other ethnic groups were sparsely represented in the ARIC study. Therefore, it is possible that the ARIC score will not apply to other US populations [77]	Met the CRP, was not cost-effective, and including clinically insignificant components may impact its performance in Africa Limited application to African populations
NHANES I Follow-Up Study Cohort [78]	Laboratory-based model: Age, sex, systolic blood pressure, smoking status, total cholesterol, reported diabetes status, current treatment for hypertension Non-laboratoy-based model: Age, sex, systolic blood pressure, smoking status, BMI, reported diabetes status, current treatment for hypertension	This study represents a population from the USA, and the proposed risk score may not be as useful in developing countries [78] Only a few low-income countries have cohort data to estimate [78] The basis for excluding HDL is not understood, i.e., lack of stratification of risk factors [78]	Met the CRP, cost-effective but including clinically insignificant variables may affect its performance in Africa Limited application to African populations Cumulative risk point less than CRP hence may perform suboptimally in Africa

Table 5 (continued)

Risk assessment tool	Component factors	Criticism	The implication of the criticism versus our findings
SMART-REACH [79]	Age, sex, BMI, current smoking, diabetes mellitus, history of heart failure, history of heart failure, history of atrial fibrillation, systolic blood pressure, serum creatinine concentration, number of locations of CVD (cerebrovascular, coronary, and peripheral artery disease) and total and low-density lipoprotein cholesterol)	Missing data for clinical measurements at the 3-month follow-up and excluded oldest patients [79] Did not account for changes in risk factor levels over time, i.e., lack of stratification of risk factors [79]	Met the CRP but not cost-effective Limited application to African populations
Novel Afrocentric model [4]	Baseline age, income < USD 100, no formal education, hypertension, dyslipidemia, diabetes mellitus, cardiac disease, family history of cerebrovascular, obesity, stress, added salt, low consumption of leafy green vegetables, regular sugar consumption, meat consumption, and physical inactivity	The model is Afrocentric but noninclusive; only data from West Africa (Nigeria & Ghana) were included Inclusion of many factors may make model administratively heavy	Met CRP but not cost-effective and time-consuming

$^{\$}$,US dollar, *CRP* critical risk point, *BMI* body mass index, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *BP* blood pressure, *ECG* electrocardiogram factor for stroke [105]. Additionally, diabetes can lead to high LDL ("bad" cholesterol) and low HDL ("good" cholesterol) levels, further increasing stroke risk [106]. Diabetes also disrupts blood clotting, increasing the risk of thrombotic events such as ischemic strokes [107] and increasing the risk of peripheral artery disease, which impairs blood flow to the limbs [108]. Diabetes is included in stroke prediction models such as the Framingham risk score, PROCAM, Reynolds risk score, ASSIGN, CUORE, QRISK, and self-reported stroke risk stratification, indicating clinical relevance. Diabetes screening is routinely performed and cost-effective, making it a suitable risk factor for predictive models; diabetes alone does not meet the critical risk point and is relevant only when combined with other risk factors in a multivariable manner.

In Africa, HIV was identified as a risk factor, with a Ri of 0.67, indicating that 67% of the studies included in this review identified HIV as a risk factor for stroke. HIV-infected individuals are 2.5 times more likely to develop stroke than those without HIV. However, the predictive significance of HIV has emerged only alongside other major risk factors, as previously noted [60]. In antiretroviral-naive populations, HIV independently increases stroke risk [109]. The contributing factors include inflammation, coagulation issues, and side effects of antiretroviral therapy on cardiovascular health [109–111]. Surprisingly, no current prediction models incorporate HIV status despite its low investigative cost. The prevalence of HIV in Africa, coupled with its low investigative cost, makes it suitable for inclusion in models for predicting the risk of stroke among populations in Africa.

In our study, age did not emerge as a risk factor for stroke in Africa and was excluded from our models. This contrasts with Western and Chinese studies [61, 65, 69, 70, 74–79], which consider age to be a significant risk factor for stroke risk. While these studies link advanced age to increased stroke risk, the studies included in this meta-analysis revealed similar stroke incidence rates among young and older adults in Africa. Stroke in young people is defined as occurring in those under age 50 [112, 113]. Our findings align with those of Sarfo et al. [114], who reported that younger stroke onset in Africa was associated with poor long-term outcomes, possibly due to a growing young population with HIV and increasing cardiovascular risk factors [101, 115]. The nonsignificance of age as a predictive factor may reflect the actual burden of HIV and cardiovascular risk factors in Africa. Stroke screening in Africa should thus not be limited on the basis of age.

Limitations

This study had several limitations. Seven of the 12 biomarkers showed variable risk estimates across studies. Publication bias influenced risk estimates for smoking and age. Subjective judgment in determining critical risk introduces a trade-off between sensitivity and specificity, necessitating the validation of models to confirm the optimal risk point and assess diagnostic performance, feasibility, and acceptability. Our findings depend heavily on data availability, raising concerns. Extensive efforts were made to search key databases, focusing on English and French, the region's main research languages. The combination of ischemic and hemorrhagic strokes in most studies is another limitation. Some articles might have been missed despite including factors with a high propensity for each stroke type. As new data emerge, CAPMAS 1 and 2 will require revisions. Additionally, regional disparities in healthcare practices and quality, which affect the quantification of laboratory-based factors, may contribute to study limitations.

Conclusions

The CAPMAS 1 and CAPMAS 2 models are promising stroke prediction models for Africa and require immediate validation. The lack of studies on specific sub-African ethnicities restricts a detailed analysis by ethnicity. However, the uniformity of stroke etiology across Africa supports a continent-wide stroke prevention policy, potentially freeing funds for development.

Recommendations

Future research should investigate ischemic and hemorrhagic stroke seperately and include subAfrican ethnic and ancestral clusters to enhance clinical prediction. The limited data on stroke risk factors in southern Africa calls for regional agencies to support multinational research. Upon validation, CAPMAS 1 and 2 should be implemented at the regional level, potentially freeing funds for development. The framework employed in this study could be adopted to study noncommunicable diseases of importance in the African context.

Abbreviations

CAPMS	Cost-effective Afrocentric predictive model for stroke
Rw	Risk weight
Ri	Risk stability index
LMIC	Low- and middle-income country
HIC	High-income country
PECOT	Population, exposure, comparison, outcome, and timeframe
OR	Odds ratio
CRP	Critical risk point
CMA	Comprehensive meta-analysis
HDL	High-density lipoprotein
CVD	Cardiovascular disease
LDL	Low-density lipoprotein

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

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Authors' contributions

NM and PO conceived the study. NM and MSB conducted the searches. OP downloaded the studies and conducted initial screening under the supervision of MN. MN and GN contributed to content reading. NM and OP ran the analysis. NP and IS revised the manuscript for intellectual contents. PO and UM conducted quality appraisal. The manuscript was drafted by NM, PO and UM. All authors read through and approved the final draft of the manuscript.

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Data availability

The review data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

In this study, ethical clearance was not needed, as there was no contact with patients. The study data were derived from primary studies in which ethical clearance and consent were obtained from the institutional review boards and individual patients. Moreover, the investigation price associated with laboratory-based risk factors was not patient or personal data but marketing data; hence, ethical clearance and consent were unnecessary [116].

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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